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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,989	11/13/2001	Michael Brown	108172-00072	6030

4372 7590 02/25/2003

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EXAMINER

JOHANNSEN, DIANA B

ART UNIT PAPER NUMBER

1634

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/986,989	<b>Applicant(s)</b> BROWN ET AL.	
	<b>Examiner</b> Diana B. Johannsen	<b>Art Unit</b> 1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 January 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)              | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4</u> . | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Priority***

1. The instant application claims benefit under 35 U.S.C. 119(e) of U.S. provisional application no. 60/247,951, filed November 13, 2000. However, claim 1, which is now pending and under consideration, is not entitled to the filing date of the provisional application. While the provisional application does disclose data from a trial in which hypertensive subjects performed "short-term exercise training consisting of 7 consecutive days of treadmill walking and/or stationary cycling for 50 min/day at 65% heart rate reserve," the '951 application does not refer to "limited exercise training" or provide a definition of any type of "exercise training" that corresponds to the broad definition of "limited exercise" provided in the instant specification. Accordingly, the effective filing date of instant claim 1 is the filing date of the instant application, i.e., November 13, 2001 (see *Hunt Co. v Mallinckrodt Chemical Works*, 177 F.2d 583,587, 83 USPQ 277, 281; MPEP 201.11).

### ***Information Disclosure Statement***

2. Regarding the PTO-1449 filed January 30, 2002, it is noted that the examiner has completed the citation for document "AM" by providing the pertinent page numbers for the reference.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing sodium excretion levels in a hypertensive human subject comprising identifying a hypertensive human subject having the human angiotensin converting enzyme gene II genotype exemplified in the specification and engaging the subject "in limited exercise training for a period of time sufficient to increase sodium excretion levels," does not reasonably provide enablement for methods of increasing sodium excretion levels in any type of hypertensive subject comprising identifying "an II genotype for an angiotensin converting enzyme gene" prior to engaging the subject in limited exercise training, as recited in the claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claim.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

Instant claim 1 is drawn to a method of "increasing sodium excretion levels in a hypertensive subject" comprising identifying a hypertensive subject having "an II genotype for an angiotensin converting enzyme gene, wherein the subject is in need of increased sodium excretion levels" and engaging the subject "in limited exercise training for a period of time sufficient to increase sodium excretion levels." It is noted that "limited exercise" is defined at page 4 of the specification as "about 5-9 single courses of exercise, preferably about 6-8, or 7 single courses of exercise" over an exercise period that is "preferably about 5-30 days, more preferred about 5-20 days, most preferred about 5-12 days," and that a "single course of exercise" is defined as "a cardiovascular exercise session of any type which is conducted during one day" (see page 4). The specification provides evidence that hypertensive human subjects having the particular angiotensin converting gene II genotype exemplified in the specification exhibit a greater increase in sodium excretion, as compared to hypertensive humans lacking the II genotype, when engaged in limited exercise (see Figures 1-2 and Examples 1-2).

It is unpredictable as to whether one of skill in the art could use applicants' invention in a manner reasonably commensurate with the claims. First, as discussed in paragraph 6, below, the instant claim is not clearly limited to the particular angiotensin converting enzyme gene exemplified in the specification. Further, the instant claim as written is sufficiently broad so as to encompass any type of "hypertensive subject." While applicants' specification provides evidence that hypertensive human subjects having the particular angiotensin converting gene II genotype exemplified in the

specification exhibit a greater increase in sodium excretion, as compared to hypertensive humans lacking the II genotype, when engaged in limited exercise, the specification provides no guidance with respect to how or whether the method of the invention might be practiced using other angiotensin converting enzyme genes found in humans and in other mammals, and/or with respect to whether the method may actually be employed successfully in hypertensive non-human subjects. Lacking guidance from the specification, one of skill in the art may look to the teachings of the prior art for further guidance and enablement of a claimed invention. It is well known to those of skill in the art that the particular angiotensin converting enzyme gene exemplified in the specification is only one of many mammalian angiotensin converting enzyme genes known in the art. For example, Donoghue et al (Circulation Research 87(5):e1-39 [9/2000]) teach a different human angiotensin converting enzyme gene, ACE2, as well as several other mammalian angiotensin converting enzyme genes (see entire reference, particular Figure 1). However, the prior art does not disclose the existence of an association between an II or equivalent genotype in any other angiotensin converting enzyme gene and improved sodium excretion following limited exercise training, either in humans or in other types of subjects. Further, the teachings of the prior art indicate that engaging a subject in exercise does not necessarily result in increased sodium excretion. For example, while Brown et al (Hypertension 30(6):1549-1553 [12/1997]) disclose an increase in sodium excretion rate in a population of hypertensive, diabetic women following 7 consecutive days of aerobic exercise (see entire reference, particularly Table 2), Kingwell et al (Medical Journal of Australia 158(4):234-238

[2/1993]), Hagberg et al (American Journal of Cardiology 64(5):348-353 [8/1989]) and Urata et al (Hypertension 9(3):245-252 [3/1987]) each provide evidence that exercise regimens that result in decreased blood pressure may have no significant effect on sodium excretion (in Kingwell et al, see entire reference, particularly page 235, left and center columns; in Hagberg et al, see entire reference, particularly page 351, left column, and Table V; in Urata et al, see entire reference, particularly Table 5).

Accordingly, the teachings of the prior art indicate that, absent evidence that a particular type of exercise regimen results in increased sodium excretion in a particular population, it is unpredictable as to whether such an increase will actually occur. Given the high skill level of one of skill in the relevant art, it is well within the ability of such an artisan to conduct further experimentation in order to determine whether a relationship exists between an II or equivalent genotype in other human or animal angiotensin converting enzyme genes and increased sodium excretion following limited exercise. However, as the outcome of such experimentation cannot be predicted, it is unknown and unpredictable as to whether any quantity of experimentation would be sufficient to enable one of skill to practice methods of increasing sodium excretion levels in which populations other than the particular human populations exemplified in the specification are engaged in "limited exercise." Accordingly, while the teachings of the specification enable one of skill in the art to practice methods of increasing sodium excretion levels in a hypertensive human subject comprising identifying a hypertensive human subject having the human angiotensin converting enzyme gene II genotype exemplified in the specification and engaging the subject "in limited exercise training for a period of time

sufficient to increase sodium excretion levels," it would require undue experimentation to use applicants' invention in a manner reasonably commensurate with claim 1. It is noted that this rejection could be overcome by amending the claim so as to limit it to hypertensive human subjects and to the particular angiotensin converting enzyme gene II genotype exemplified in the specification.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite over the recitation of the limitation "an II genotype for an angiotensin converting enzyme gene." While there is a particular human angiotensin converting enzyme gene II genotype known in the art and discussed in the specification, the wording of the claim does not make clear whether the claim is intended to be limited to this particular gene and genotype, or whether the claim is intended to encompass "II" genotypes or equivalents thereof that may be found in other known human angiotensin converting enzyme genes (e.g., the human ACE2 gene), and/or in one or more of the many other angiotensin converting enzyme genes of other types of subjects (e.g., hypertensive non-human mammals) that are known in the art. As this recitation does not make clear what gene or genes are intended to be encompassed by the claim, the metes and bounds of the claim are unclear.



***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Hagberg et al (WO 99/45383 A1 [9/1999]).

Claim 1 is drawn to a method of "increasing sodium excretion levels in a hypertensive subject" comprising identifying a hypertensive subject having "an II genotype for an angiotensin converting enzyme gene, wherein the subject is in need of increased sodium excretion levels" and engaging the subject "in limited exercise training for a period of time sufficient to increase sodium excretion levels." It is noted that "limited exercise" is defined at page 4 of the specification as "about 5-9 single courses of exercise, preferably about 6-8, or 7 single courses of exercise" over an exercise period that is "preferably about 5-30 days, more preferred about 5-20 days, most preferred about 5-12 days," and that a "single course of exercise" is defined as "a cardiovascular exercise session of any type which is conducted during one day" (see page 4).

Hagberg et al disclose a method that may be employed to reduce the blood pressure of hypertensive individuals, which method requires steps of identifying subjects who are in need of a reduction in blood pressure who have an angiotensin converting enzyme gene II genotype, and engaging those subjects in "moderate

exercise training" (see entire reference, particular page 6, lines 13-23; page 7, lines 6-11; Example 5; claim 8). The definition of "limited exercise" in the instant specification (see page 4) is nearly identical to the definition of "moderate exercise" taught by Hagberg et al (see page 3, lines 13-17); the definitions require the same number of "single courses of exercise," and differ only in that the exercise period for moderate exercise as defined in Hagberg et al "may be from about 5-50 days, preferably from about 5-30 days, 5-20 days, or 5-15 days," while the period for "limited exercise" as defined in the instant specification lacks the limitation "from about 5-50 days," and recites "preferably 5-30 days, most preferred about 5-20 days, most preferred about 5-12 days." Accordingly, while the "engaging" step of instant claim 1 is not identical in scope to that of Hagberg et al, instant claim 1 encompasses methods in which both "identifying" and "engaging" steps as disclosed in Hagberg et al are performed.

While instant claim 1 is drawn to a method "of increasing sodium excretion levels in a hypertensive subject" in which a subject "in need of increased sodium excretion levels" is engaged "in limited exercise training for a period of time sufficient to increase sodium excretion levels in the subject," the method steps of the method taught by Hagberg et al are nearly identical to, and are encompassed by, those of instant claim 1. Thus, performance of the method disclosed by Hagberg et al and exemplified in Example 5 of Hagberg et al (in which hypertensive subjects having an II genotype of an angiotensin converting enzyme gene are engaged in a course of exercise meeting the definition of "limited exercise" in the instant specification), would inherently result in "increasing sodium excretion levels in a hypertensive subject." The increase in sodium

excretion referred to in instant claim 1 is merely a previously unrecognized benefit that necessarily results from the performance of the method steps disclosed and exemplified by Hagberg et al; this benefit is inherent and therefore does not distinguish the method of instant claim 1 from that taught by Hagberg et al. Accordingly, Hagberg et al anticipate the claimed invention.

### ***Double Patenting***

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of U.S. Patent No. 6,399,306 B1. An obviousness type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). In the instant case, although the conflicting claims are not identical, they are not patentably distinct from each other because claim 8 of the '306 patent anticipates instant claim 1.

Instant claim 1 and claim 8 of the '306 patent are each drawn to a method requiring steps of identifying subjects who are in need of a reduction in blood pressure who have an angiotensin converting enzyme gene II genotype, and engaging those subjects in a particular type of exercise for a particular period of time. Regarding the "identifying" step of the claims, it is noted that instant claim 1 recites a "hypertensive subject," while claim 8 of the '306 patent recites a subject "in need of reduced blood pressure levels." However, it is an inherent property of a "hypertensive subject" that he/she constitutes a subject in need of reduced blood pressure; further, it is an inherent property of a subject "in need of reduced blood pressure levels" that he/she is hypertensive (i.e., has blood pressure that is higher than that which is desired). Further, each "identifying" step is performed on a subpopulation of subjects having the same genotype (specifically, an angiotensin converting gene II genotype). Regarding the

"engaging" step, in the case of instant claim 1, the subject is engaged in "limited exercise training," whereas in claim 8 of the '306 patent the subject is engaged in "moderate exercise training." However, the definition of "limited exercise" in the instant specification (see page 4) is nearly identical to the definition of "moderate exercise" in the specification of the '306 patent (see column 2, lines 37-42); the definitions require the same number of "single courses of exercise," and differ only in that the exercise period for moderate exercise as defined in the '306 patent "may be from about 5-50 days, preferably from about 5-30 days, 5-20 days, or 5-15 days," while the period for "limited exercise" as defined in the instant specification lacks the limitation "from about 5-50 days," and recites "preferably 5-30 days, most preferred about 5-20 days, most preferred about 5-12 days." Accordingly, while the "engaging" step of instant claim 1 is not identical in scope to that of claim 8, instant claim 1 encompasses methods in which both "identifying" and "engaging" steps as recited in claim 8 of the '306 patent are performed.

While instant claim 1 is drawn to a method "of increasing sodium excretion levels in a hypertensive subject" in which a subject "in need of increased sodium excretion levels" is engaged "in limited exercise training for a period of time sufficient to increase sodium excretion levels in the subject," the method steps of claim 8 of the '306 patent are nearly identical to, and are encompassed by, those of instant claim 1, as discussed above. Thus, performance of the steps of claim 8 of the '306 patent, and particularly the "moderate exercise training" required by claim 8, would inherently result in "increasing sodium excretion levels in a hypertensive subject." The increase in sodium excretion

referred to in instant claim 1 is merely a previously unrecognized benefit that necessarily results from the performance of the invention of claim 8 of the '306 patent; this benefit is inherent and therefore does not distinguish the method of instant claim 1 from that of '306 claim 8. Accordingly, the claims are not patentably distinct from one another, as claim 8 of the '306 patent anticipates instant claim 1.

**Conclusion**

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

A handwritten signature in black ink, appearing to read "Diana B. Johannsen", with a long, sweeping horizontal line extending to the right.

Diana B. Johannsen  
February 24, 2003